THE OHIO STATE UNIVERSITY
COLUMBUS

DEPARTMENT OF MEDICINE
OFFICE AND RESEARCH LABORATORIES
KINSMAN HALL

Y
SABIN
(DOAN)

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Dear Dr. Sabin:

I hope you have received my letter dictated in between the end of our Post-Graduate Seminar here and my going to Cleveland.

Your two letters following the telegram and the train letter were awaiting me when I got back Saturday morning from Cleveland. I am sure you will have interpreted the very deep satisfaction that we all had in your continuing interest in our little patient with the peculiar bone marrow and blood picture, and there was, of course, no thought other than to get at the true source of the granular cytoplasmic material we found in the blood.

When we had the opportunity of studying the Wright's-Giemsa and Kingsley stains of the marrow films, we found a disconcerting number of basophil staining granular materials in many of the abnormal cells. There had been no suggestion in the supravitally stained preparations of true basophil granulation, and I had not recorded in my differential count, any excess of basophil granule myelocytes. The cytoplasmic masses I originally called blood platelets in the blood, both supravitally and in the fixed film, showed a rather deeply neutral red staining granular material similar to that found in the marrow cells. Dr. Wiseman, in studying this material, was inclined to feel that we had here the fourth in our series of basophil granule leucemias, but some of the rest of us felt that this was not true basophil granulation, but rather abnormal or toxic variables in the megakaryocytic granulations.

The second bone marrow supravital study which was made just before I left for Cleveland, again did not reveal any true basophil granule myelocytes in excess. On careful study there were some cells with vesicular nuclei and large nucleoli that took a suggestive magenta red stain, which probably represented a correlation with the basophil granule-like reaction in the fixed films. There was, of course, a definite left shift in the myeloid cells, and we felt we could identify a certain number of myeloblasts, as distinct however, from other non-myeloblastic primitive cells, that I still felt were related by a direct transition of forms to a definitely increased proportion of unquestionable megakaryocytes which were again found in the marrow. Here was a situation in which we felt definitely that Dr. Houghton's tissue culture technic might be of distinct help. He therefore was prepared to culture the marrow removed under sterile precautions on our second sternal puncture, and I think the subsequent course of events practically completely confirms the fundamental pathology as primarily affecting the megakaryocytic elements.

On last Saturday, five days after the cultures were made, all preparations showed every stage of megakaryocytic maturation with most bizarre, mitotic figures scattered frequently among this cell type. Today, again we have studied the cultures, and small, intermediate and large mononuclear, polynuclear and multinuclear megakaryocytes of unquestioned identity dominate the cultures. Miss Melvin is now drawing one medium sized megakaryocyte with 5 different separate nuclei in mitotic division. We saw one last Saturday with 2 nuclei quiescent and a third

nucleus in mitosis in the same cell.

The fixed sections have come through on the first marrow removed by sternal puncture, and show an unquestioned hyperplasia with left shift of the megakaryocytic cells, and the mononuclear young cells are in close association with, and are morphologically similar to, typical megakaryocytes.

The lad is still in the hospital, and we are continuing to follow him without any quantitative change in the peripheral blood level, either red blood cells or white cells. The relative benignity of the process since the first symptoms appeared 10 months ago and continuing to the present time, is distinctly against a basophil granulocyte leucemia, at least in our experience to date.

I had read Menkins' note in Science for March 29th, and, as you surmised, have been very much interested in this present communication suggesting that leucocyte stimulating material in his inflammatory exudates is either a globulin or is closely associated with a pseudo-globulin fraction. I should like to try this material on the hypoplastic marrow of the starved pigeon. I feel, as you know, that this represents one of the best in vivo test tubes for assaying the fundamental stimulatory potency of any substance which is said to have a fundamental stimulatory influence on either erythropoiesis or myelopoiesis. It would be of interest also, of course as you suggest, to have Dr. Houghton study its cell stimulating potency in cell cultures.

It is indeed interesting to note how many different observations are appearing which either directly or indirectly substantiate your conception with reference to the R. E. system.

You will be interested in knowing, that while in Cleveland last week, I was greeted on every hand with favorable comments with reference to the Post-Graduate Course given the week previously, there having been apparently, a unanimity in the enthusiastic report made by each of the men to his friends after they all got to Cleveland.

You will have received a copy of the expression of appreciation which the men presented to the faculty of the course at its conclusion. I am so glad that you were able to make the very large personal contribution to the success of the undertaking.

I am going to take some pictures of the children this spring as soon as the weather gets a little better, and I shall certainly look forward to sending them to you when they become available. I am glad you want a snap of Ellen and Elizabeth as they are now.

All send affectionate greetings,

D-H

Charles

Charles A. Doan, M. D.
Professor of Medicine

Dr. Florence R. Sabin,
1333 E. 10th Avenue,
Denver, Col.